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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/648,270 05/15/96 TOR

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EXAMINER

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ART UNIT

PAPER NUMBER

1623

28

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

08/648,270

Applicant(s)

Tor et al.

Examiner

L. E. Crane

Group Art Unit

1623

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ----3---- MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on 04/21/2000 (M Amdt F)-----
- ☒ This action is FINAL.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

- ☒ Claim(s) 44-49 -----is/are pending in the application.
- Of the above claim(s)----- is/are withdrawn from consideration.
- ☐ Claim(s)----- is/are allowed.
- ☐ Claim(s)----- is/are rejected.
- ☐ Claim(s)----- is/are objected to.
- ☐ Claim(s)----- are subject to restriction or election requirement.
- ☒ Claims 27-~~4~~ 43 have been cancelled.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
- ☐ received in Application No. (Series Code/Serial Number)_____.
- ☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received:_____.

Attachment(s)

- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s)._____ ☐ Interview Summary, PTO-413
- ☐ Notice of Reference(s) Cited, PTO-892 ☐ Notice of Informal Patent Application, PTO-152
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948 ☐ Other_____

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The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group 1600, Art Unit 1623.

- 5 Claims 27-43 have been cancelled, claims 44-46 have been amended, and new claims 48-49 have been added as per the amendment filed April 21, 2000.

Claims 44-49 remain in the case.

- 10 Claims 44-49 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 44-46 and 48 the subject matter of the instant claims is indefinite because the attachment point or attachment points of the "Z" substituent have not been defined.

- 15 Applicant's arguments filed April 21, 2000 have been fully considered but they are not persuasive.

- 20 Applicant has argued that the specification at pages 24-32 provides adequate guidance concerning the attachment of nucleoside, nucleotide and oligonucleotide/nucleic acid/nucleic acid analog attachment. Examiner agrees that a prospective disclosure is where applicant indicates, but examiner is looking for specific embodiments. There are no specific embodiments which provide complete directions to achieve the synthesis of any one of the compounds of the instant claims. As noted in *Brenner v. Manson* (148 USPQ 689; S. Ct. 1966) a patent is "... not a hunting licence."

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Claims 26-47 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In claims 44-49 the subject matter is directed to a vast array of substituent moieties but applicant's disclosure is limited in its specific embodiments to substituted nucleosides, substituted nucleotides, and substituted nucleoside phosphoramidites and nucleic acid sequences including a substituted nucleoside. For example, in claim 44, line 5, the term "M is a transition metal ion" is lacking in enabling support within the instant disclosure in the form of any showing that applicant had possession of compounds of the kind indicated, that a substantial number of transition metal complexes had actually been made, and that the method of making described in sufficient detail to permit the ordinary practitioner to know how to make said compounds based on contents of the instant disclosure. Previous policy guidance on enablement to the effect that the "law requires that disclosure in an application shall inform those skilled in the art how to use appellant's alleged discovery, not how to find out how to use it for themselves" (*In re Gardner et al.*, 166 USPQ 138 (CCPA 1970)), has apparently become the judicial policy of the successor (CAFC) court. Examiner refers applicant to the recent April, 1999 ABA meeting in Washington, DC and the Program Book therefrom wherein numerous appellate practitioners reported that claims lacking proper enabling support were being dispatched by that court to the circular file via findings of invalidity, a policy which the practitioners promised is in the process of being extended by the CAFC to all subject matter areas. Therefore, examiner respectfully suggests that the instant claims be

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redrafted with this policy in mind, and that additional data if available be added in CIP filings as appropriate to support claims drafted to include presently non-enabled subject matter.

5 Applicant's arguments filed April 21, 2000 have been fully considered but they are not persuasive.

10 Applicant has alleged that examiner has admitted that nucleosides, nucleotides, substituted nucleotide phosphoramidites and nucleic acid sequences are enabled. Examiner clarifies the previous office action as follows: examiner noted that the disclosure describes the noted subject matter, but herein notes that the descriptions are in each case entirely
15 prospective. Examiner also argues herein that this is not adequate to enable the instant claimed subject matter because the prospective disclosure is not further supported by any specific exemplifications and therefore the ordinary practitioner would have to expend undue
20 experimentation to carry out the instant claimed invention because of the complete absence of requisite guidance within the instant disclosure. Therefore the instant grounds of rejection will not be withdrawn, and has been maintained for the reasons noted.

25 Applicant has argued that the enablement requirement is the ability of " ... one skilled in the art to make and use the description of the invention to make and use the claimed invention without undue experimentation," further quoting a Fed Circuit opinion to the effect that every detail need not be included because the inventor is speaking to one ordinary skill. Unfortunately, applicant has left out details which suggest
30 that the invention as described has been executed as claimed. For example, there appear three structures which provide prospective support for synthetic precursors for the instant claimed subject matter, but

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inspection further in the disclosure wherein specific examples are delineated fails to provide any guidance of any kind concerning how these precursors were synthesized and how they were subsequently transformed into the compounds of the instant claims. Applicant is reminded that a

5 patent application is not a research proposal, but is the basis of a patent grant only in recognition of what applicant has provided in the form of a real contribution to the art which can be reproduced by the ordinary practitioner. While the instant disclosure contains many prospective disclosures based on the theory that the existing prior art is sufficient to

10 guide the ordinary practitioner in the manner suggested by applicant's argument, prospective disclosures alone are inadequate in the instant art area because nucleosides and particularly nucleotides and oligonucleotides are notoriously well known in the art to be polydentate ligands and therefore capable of coordinating in many ways with a transition metal

15 ion. Therefore, examiner maintains that a description of how to make specific exemplifications is essential in the instant case to meet the enablement requirement. Applicant is referred to *Ex parte Balzarini et al.* at 21 USPQ 2d 1892, 1894 et seq (1990) wherein the BPAI makes it clear that enablement in the areas of the biochemical sciences with potential

20 medicinal applications must be based on results that are more than prospective. For these reasons the instant rejection has been maintained.

Claims 44-49 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

25 the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 44-49 are broadly descriptive of the claimed invention, but the specific embodiments teach with a very small number of example how

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the instant invention may be carried out, but no examples which disclose how to incorporate the instant claimed compounds into an oligonucleotide. Additionally, there are no examples which disclose how to make any of the requisite intermediate nucleoside and nucleotide-precursor compounds numbered "9," "10," "11" and "12" in the disclosure at pp. 12-13. For these reasons the exemplifications included within instant claims 44-49 are deemed to represent subject matter which would require undue experimentation by the ordinary practitioner to determine how to make said compounds, and that therefore said claims lack adequate enabling support within the instant disclosure.

Applicant's arguments filed April 21, 2000 have been fully considered but they are not persuasive.

Applicant has noted the Forman factors recapitulate in *In re Wands*. Applicant has argued that the quality of experimentation necessary factor "is not great" based on applicant's conclusion that "[p]alladium-mediated cross coupling reactions are well known to be versatile." Applicant then concludes that the amount of direction or guidance present in the specification is high. As regards the third factor, applicant notes the presence of some working examples as an adequate basis for a finding that the claimed invention is enabled. As regards the fourth factor, applicant notes that bromination of the 3- and 8-positions of phenanthrolines as shown by instant exemplifications is an adequate basis for concluding that the instant claims are enabled. As regards the fifth and sixth factors, applicant concludes that the state of the prior art and the relative skill of the ordinary practitioner are both "high" which applicant finds also supports a finding that the instant claims are enabled. As regards the seventh factor, applicant's conclude that the generation of 3- and/or 8-substituted phenanthrolines provide an adequate basis for a finding that

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many compounds are enabled. And as regards the eighth factor, applicants conclude that the breadth of the claims is appropriate is consistent with a finding that the claimed subject matter is adequately enabled.

5 Examiner respectfully disagrees with applicant's reasoning and conclusions concerning factors 1-8.

10 As regards factor 1, applicant has not disclosed any synthesis which reaches any one of the compounds the structures of which are provided at page 12 of the disclosure, let alone compounds wherein the phenanthroline substituent has been complexed with any metal ion. In view of the number of heteroatoms (N and O are potential ligands) in a nucleoside and the even greater number in a nucleotide, it is not clear to the instant examiner that the synthesis of any exemplification of any one of the instant claims will be straightforward. For this reason examiner finds that the level of experimentation will be undue.

15 As regards factor 2, the guidance provided herein is minimal, with no specific embodiment (written description of how a compound was actually synthesized) having been provided which is included within the scope of any instant claim.

20 As regards factor 3, applicant has provided no working exemplification wherein any one claimed compound has been synthesized.

As regards factor 4, applicant has made some substituted 1,10-phenanthroline but has completely failed to show how to incorporate these phenanthrolines or metal chelates thereof as a substituent at any position of any nucleoside, nucleotide, nucleic acid, or nucleic acid analogue.

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As regards factor 5, the prior art does not provide any guidance directed to how to make compounds of the kind claimed, e.g. 1,10-phenanthroline-chelate-substituted purine or pyrimidine nucleosides/nucleotides/nucleic acids/nucleic acid analogues. Therefore, the prior art fails to provide the minimum requisite guidance needed to execute the instant invention.

As regards factor 6, the relative skill of the ordinary practitioner is a reflection of the published art. Therefore, in light of the absence of relevant prior art to guide the ordinary practitioner, the level of skill is properly found to be low.

As regards factor 7, the synthesis of nucleosides is well known but the synthesis of nucleosides, nucleotides or nucleic acids/nucleic acid analogues with phenanthroline substituents or chelates thereof is not a area of nucleoside/nucleotide synthesis which is presently well known or well understood by any practitioner.

As regards factor 8, the claims are directed to a vast array of compounds the precise structures of which are not well defined, which is deemed to be a reason to find the claims lacking in enablement because not one complete synthesis of one of the compounds claimed has been disclosed herein.

Examiner therefore concludes that the instant claims are not enabled because applicant

- i) has not disclosed in any figure in in any written description how to make and/or use any single claimed compound, and
- ii) has not provided a clear exposition of wherein the prior art guidance may be found to make any one of the claimed compounds.

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For these reasons including examiner's analysis of the claims in light of the Forman factors, examiner concludes that the instant claimed invention is lacking in adequate enabling support in the form of examples of how to make and in the form of descriptions of complete synthetic protocols leading to any one of the compounds claimed. Therefore, the instant grounds of rejection have been maintained.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon the filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. §1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Papers related to this application may be submitted to Group 1600 via facsimile transmission(FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone numbers for the FAX machines now


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operated by Group 1600 are (703) 308-4556 and (703) 305-3592 for Official documents. Before transmission of any Draft communications, Applicant is respectfully requested to seek instructions from instant Examiner.

- 5 Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is 703-308-4639. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

- 10 If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Gary Geist, can be reached at (703)-308-1701.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is 703-308-1235.

15 LECrane:lec
06/29/00 


GARY GEIST
SUPERVISORY PATENT EXAMINER
TECH CENTER 1600